CGCCTGTGCCCTCTGCCTGGGAGCCTGGGGCCGCCTGTCTGCGCGGTCCGGATGCGCTCAGGTCAAGGTTCCTTTCG
CGGCTGTCTCCCAAGCCCCTAACTAGTGACTTCCACTGTGGCGGGCAGGGAAGCCATTGGCAGAACCTAGCCAGTCA
GGAATCTGCATCTCTTCCCTCATTATCCTCTCCCTGGCATTGCTTTGCTCGGGTCCAGCTCAGTTGGTGACGCGGCC
CCTTCTCCCCAGGTTGGGATCCACGGAAGCAGGGGTGCAGGCCGGCCAGGCACTGTGCCATGAGCCAGAGCCCGAGG
TTCGTGACCCGGAGGGGCGGCTCTCTAAAGGCTGCCCCTGGAGCCGGCACCCGGCGCAACGAGAGCCAGGACTATTT
GCTGATGGACGAGCTGGGAGACGACGGCTACCCGCAGCTCCCGCTGCCACCGTATGGCTACTACCCCAGCTTCCGGG
GTAATGAAAACAGACTGACTCACCGGCGGCAGACGATTCTTCGTGAGAAGGGAAGAAGGTTAGCTAATCGAGGACCA
GCATACATGTTTAATGATCATTCAACAAGCCTGTCTATTGAGGAAGAACGCTTTCTAGATGCAGTTGAATATGGCAA
CATCCCAGTGGTCTGGAAGATGCTAGAAGAGTGTCATTCCCTCAATGTTAACTGTGTGGATTACATGGGCCAGAATG
CCCTACAGCTGGCTGTGGCCAATGAGCACTTGGAAATCACAGAGCTGCTACTCAAGAAGGAAAACTTGTCTCGAGTT
GGGGATGCTTTACTTTTAGCCATTAGTAAAGGTTATGTACGGATTGTGGAGGCAATCCTCAACCATCCATCTTTTGC
TGAAGGCAAAAGGTTAGCGACAAGCCCCAGCCAGTCTGAACTTCAGCAAGATGACTTTTATGCCTATGATGAAGATG
GGACGCGGTTCTCCCATGATGTGACTCCAATCATTCTCGCTGCACATTGCCAGGAATATGAAATTGTGCATACCCTC
CTGAGAAAGGGTGCCCGGATTGAGCGGCCTCATGATTACTTCTGCAAGTGTACAGAATGCAGCCAGAAGCAGAAGCA
TGATTCCTTCAGCCACTCTAGATCCAGGATCAATGCATACAAAGGTCTGGCAAGTCCAGCATACCTGTCATTGTCCA
GTGAAGATCCAGTCATGACTGCTTTAGAACTTAGCAATGAGCTGGCAGTGCTTGCCAACATTGAGAAAGAGTTCAAG
AATGACTACAGGAAGCTGTCTATGCAGTGCAAGGATTTCGTTGTTGGTCTCTTGGACCTCTGCAGAAACACAGAGGA
AGTGGAGGCCATCCTGAATGGGGATGCAGAGACTCGCCAGCCCGGGGACTTCGGCCGTCCAAATCTCAGCCGTTTAA
AACTTGCTATTAAGGATGAAGTAAAAAAATTTGTGGCTCATCCAAACTGTCAGCAACAGCTCCTGTCCATATGGTAT
GAGAACCTCTCTGGTTTACGGCAGCAGACCATGGCAGTGAAGTTCCTCGTGGTCCTTGCTGTTGCCATTGGATTGCC
CTTCCTGGCTCTCATATACTGGTGTGCTCCTTGCAGCAAGATGGGGAAGATATTGCCGAGACCGTTCATGAAGTTTG
TAGCACACGCAGCCTCCTTCACCATTTTCCTGGGGCTGCTCGTCATGAATGCAGCTGACAGATTTGAAGGCACCAAG
CTCCTCCCTAATGAAACCAGCACAGATAATGCAAGGCAGCTGTTCAGGATGAAAACATCCTGTTTCTCATGGATGGA
GATGCTCATTATATCCTGGGTAATAGGCATGATATGGGCTGAATGTAAAGAAATCTGGACTCAAGGCCCCAAAGAAT
ACTTATTTGAGTTGTGGAATATGCTTGACTTTGGAATGCTGGCAATCTTTGCAGCATCATTCATTGCAAGATTTATG
GCGTTCTGGCATGCATCCAAAGCTCAGAGCATCATTGATGCAAATGATACTTTAAAGGATTTGACAAAAGTCACACT
GGGGGACAACGTTAAATACTACAATCTGGCCAGGATAAAGTGGGACCCTACTGATCCTCAGATCATCTCTGAAGGTC
TTTATGCAATCGCTGTGGTTTTAAGTTTCTCCAGAATAGCTTACATTTTACCAGCAAATGAAAGCTTTGGACCTCTG
CAGATTTCACTTGGAAGAACAGTGAAAGATATCTTCAAATTCATGGTCATATTCATCATGGTGTTTGTAGCCTTTAT
GATTGGAATGTTCAACCTTTACTCCTACTACATTGGCGCAAAACAGAATGAAGCATTCACAACAGTTGAGGAAAGTT
TTAAGACACTGTTCTGGGCTATCTTTGGTCTTTCTGAAGTGAAGTCAGTGGTCATTAACTACAATCACAAGTTCATT
GAAAACATCGGCTACGTTCTGTATGGTGTCTATAATGTCACAATGGTCATTGTTTTGCTAAATATGTTAATTGCGAT
GATCAATAGTTCATTCCAGGAAATTGAGGATGATGCGGACGTGGAGTGGAAGTTTGCAAGGGCCAAATTGTGGTTTT
CCTACTTTGAGGAGGGGAGAACACTTCCTGTCCCCTTCAATCTTGTACCAAGTCCAAAATCCTTGCTTTATCTCCTA
TTGAAATTTAAGAAATGGATGTGTGAGCTCATCCAGGGTCAAAAGCAAGGCTTCCAAGAAGATGCAGAGATGAACAA
GAGAAATGAAGAAAAGAAATTTGGAATTTCAGGAAGTCACGAAGACCTTTCAAAATTTTCACTTGACAAAAATCAGT
TGGCACACAACAAACAATCAAGTACAAGGAGCTCAGAAGATTATCATTTAAATAGTTTCAGTAACCCTCCAAGACAA
TATCAGAAAATCATGAAGAGACTCATTAAAAGATATGTATTGCAGGCCCAGATTGATAAGGAGAGCGATGAGGTGAA
TGAAGGGGAATTGAAGGAAATTAAGCAAGACATCTCAAGTCTCCGTTATGAACTCCTTGAAGAGAAATCACAGAACT
CAGAAGACCTAGCAGAGCTCATTAGAAAACTCGGGGAGAGACTGTCGTTAGAGCCAAAGCTGGAGGAAAGCCGCAGA
TAGAGCAGAGCCCCTCAGAAGTGCATATTTATTTCTCCACTTGAAGCCATATTATTTTCTGACTTATTTTTTTAAGT
GTCAATGATAAAAAGTATGTTAACTGATAACTTGGATCATTTAGAGTCCTAATATCAAGCTTTTTGGGAGATTAAAT
TGCATTGCTGAGGGCTAACAATTGCTG (SEQ ID NO:1)

FIGURE 1

MSQSPRFVTRRGGSLKAAPGAGTRRNESQDYLLMDELGDDGYPQLPLPPYGYYPSFRGNENRLTHRRQTI
LREKGRRLANRGPAYMFNDHSTSLSIEEERFLDAVEYGNIPVVWKMLEECHSLNVNCVDYMGQNALQLAV
ANEHLEITELLLKKENLSRVGDALLLAISKGYVRIVEAILNHPSFAEGKRLATSPSQSELQQDDFYAYDE
DGTRFSHDVTPIILAAHCQEYEIVHTLLRKGARIERPHDYFCKCTECSQKQKHDSFSHSRSRINAYKGLA
SPAYLSLSSEDPVMTALELSNELAVLANIEKEFKNDYRKLSMQCKDFVVGLLDLCRNTEEVEAILNGDAE
TRQPGDFGRPNLSRLKLAIKDEVKKFVAHPNCQQQLLSIWYENLSGLRQQTMAVKFLVVLAVAIGLPFLA
LIYWCAPCSKMGKILPRPFMKFVAHAASFTIFLGLLVMNAADRFEGTKLLPNETSTDNARQLFRMKTSCF
SWMEMLIISWVIGMIWAECKEIWTQGPKEYLFELWNMLDFGMLAIFAASFIARFMAFWHASKAQSIIDAN
DTLKDLTKVTLGDNVKYYNLARIKWDPTDPQIISEGLYAIAVVLSFSRIAYILPANESFGPLQISLGRTV
KDIFKFMVIFIMVFVAFMIGMFNLYSYYIGAKQNEAFTTVEESFKTLFWAIFGLSEVKSVVINYNHKFIE
NIGYVLYGVYNVTMVIVLLNMLIAMINSSFQEIEDDADVEWKFARAKLWFSYFEEGRTLPVPFNLVPSPK
SLLYLLLKFKKWMCELIQGQKQGFQEDAEMNKRNEEKKFGISGSHEDLSKFSLDKNQLAHNKQSSTRSSE
DYHLNSFSNPPRQYQKIMKRLIKRYVLQAQIDKESDEVNEGELKEIKQDISSLRYELLEEKSQNSEDLAE
LIRKLGERLSLEPKLEESRR (SEQ ID NO:2)

FIGURE 2

underlined = deleted in targeting construct

BOLD = sequence flanking Neo insert in targeting construct

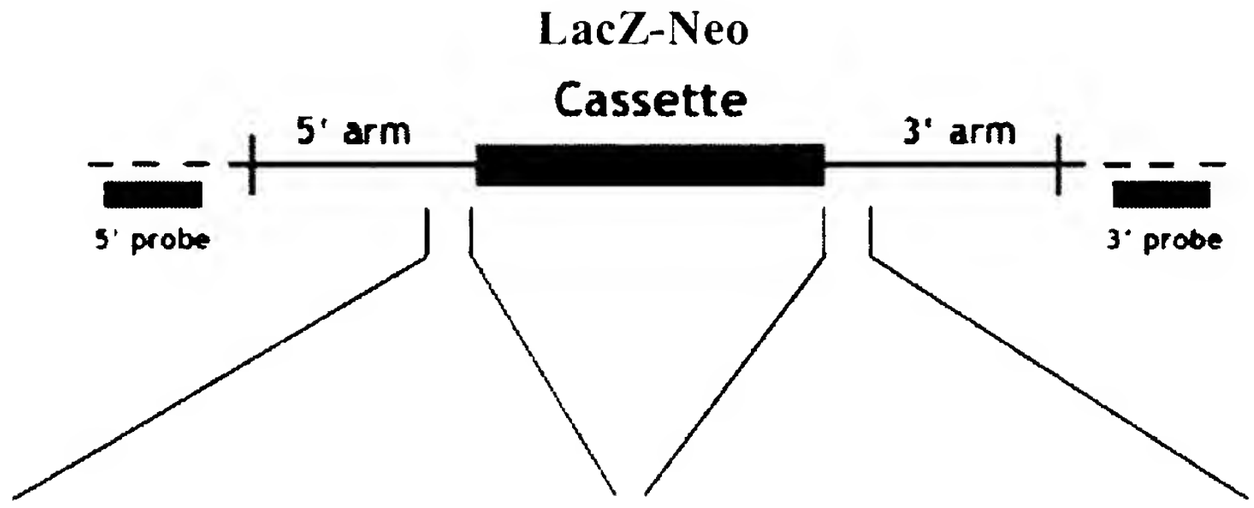
CGCCTGTGCCCTCTGCCTGGGAGCCTGGGGCCGCCTGTCTGCGCGGTCCGGATGCGCTCAGGTCAAGGTTCCT
TTCGCGGCTGTCTCCCAAGCCCCTAACTAGTGACTTCCACTGTGGCGGGCAGGGAAGCCATTGGCAGAACCTA
GCCAGTCAGGAATCTGCATCTCTTCCCTCATTATCCTCTCCCTGGCATTGCTTTGCTCGGGTCCAGCTCAGTT
GGTGACGCGGCCCCTTCTCCCCAGGTTGGGATCCACGGAAGCAGGGGTGCAGGCCGGCCAGGCACTGTGCCAT
GAGCCAGAGCCCGAGGTTCGTGACCCGGAGGGGCGGCTCTCTAAAGGCTGCCCCTGGAGCCGGCACCCGGCGC
AACGAGAGCCAGGACTATTTGCTGATGGACGAGCTGGGAGACGACGGCTACCCGCAGCTCCCGCTGCCACCGT
ATGGCTACTACCCCAGCTTCCGGGGTAATGAAAACAGACTGACTCACCGGCGGCAGACGATTCTTCGTGAGAA
GGGAAGAAGGTTAGCTAATCGAGGACCAGCATACATGTTTAATGATCATTCAACAAGCCTGTCTATTGAGGAA
GAACGCTTTCTAGATGCAGTTGAATATGGCAACATCCCAGTGGTCTGGAAGATGCTAGAAGAGTGTCATTCCC
TCAATGTTAACTGTGTGGATTACATGGGCCAGAATGCCCTACAGCTGGCTGTGGCCAATGAGCACTTGGAAAT
CACAGAGCTGCTACTCAAGAAGGAAAACTTGTCTCGAGTTGGGGATGCTTTACTTTTAGCCATTAGTAAAGGT
TATGTACGGATTGTGGAGGCAATCCTCAACCATCCATCTTTTGCTGAAGGCAAAAGGTTAGCGACAAGCCCCA
GCCAGTCTGAACTTCAGCAAGATGACTTTTATGCCTATGATGAAGATGGGACGCGGTTCTCCCATGATGTGAC
TCCAATCATTCTCGCTGCACATTGCCAGGAATATGAAATTGTGCATACCCTCCTGAGAAAGGGTGCCCGGATT
GAGCGGCCTCATGATTACTTCTGCAAGTGTACAGAATGCAGCCAGAAGCAGAAGCATGATTCCTTCAGCCACT
CTAGATCCAGGATCAATGCATACAAAGGTCTGGCAAGTCCAGCATACCTGTCATTGTCCAGTGAAGATCCAGT
CATGACTGCTTTAGAACTTAGCAATGAGCTGGCAGTGCTTGCCAACATTGAGAAAGAGTTCAAGAATGACTAC
AGGAAGCTGTCTATGCAGTGCAAGGATTTCGTTGTTGGTCTCTTGGACCTCTGCAGAAACACAGAGGAAGTGG
AGGCCATCCTGAATGGGGATGCAGAGACTCGCCAGCCCGGGGACTTCGGCCGTCCAAATCTCAGCCGTTTAAA
ACTTGCTATTAAGGATGAAGTAAAAAAA**TTTGTGGCTCATCCAAACTGTCAGCAACAGCTCCTGTCCATATGG**
TATGAGAACCTCTCTGGTTTACGGCAGCAGACCATGGCAGTGAAGTTCC**TCGTGGTCCTTGCTGTTGCCATTG**
GATTGCCCTTCCTGGCTCTCATATACTGGTGTGCTCCTTGCAGCAAGATGGGGAAGATATTGCCGAGACCGTT
CATGAAGTTTGTAGCACACGCAGCCTCCTTCACCATTTTCCTGGGGCTGCTCGTCATGAATGCAGCTGACAGA
TTTGAAGGCACCAAGCTCCTCCCTAATGAAACCAGCACAGATAATGCAAGGCAGCTGTTCAGGATGAAAACAT
CCTGTTTCTCATGGATGGAGATGCTCATTATATCCTGGGTAATAGGCATGATATGGGCTGAATGTAAAGAAAT
CTGGACTCAAGGCCCCAAAGAATACTTATTTGAGTTGTGGAATATGCTTGACTTTGGAATGCTGGCAATCTTT
GCAGCATCATTCATTGCAAGATTTATGGCGTTCTGGCATGCATCCAAAGCTCAGAGCATCATTGATGCAAATG
ATACTTTAAAGGATTTGACAAAAGTCACACTGGGGGACAACGTTAAATACTACAATCTGGCCAGGATAAAGTG
GGACCCTACTGATCCTCAGATCATCTCTGAAGGTCTTTATGCAATCGCTGTGGTTTTAAGTTTCTCCAGAATA
GCTTACATTTTACCAGCAAATGAAAGCTTTGGACCTCTGCAGATTTCACTTGGAAGAACAGTGAAAGATATCT
TCAAATTCATGGTCATATTCATCATGGTGTTTGTAGCCTTTATGATTGGAATGTTCAACCTTTACTCCTACTA
CATTGGCGCAAAACAGAATGAAGCATTCACAACAGTTGAGGAAAGTTTTAAGACACTGTTCTGGGCTATCTTT
GGTCTTTCTGAAGTGAAGTCAGTGGTCATTAACTACAATCACAAGTTCATTGAAAACATCGGCTACGTTCTGT
ATGGTGTCTATAATGTCACAATGGTCATTGTTTTGCTAAATATGTTAATTGCGATGATCAATAGTTCATTCCA
GGAAATTGAGGATGATGCGGACGTGGAGTGGAAGTTTGCAAGGGCCAAATTGTGGTTTTCCTACTTTGAGGAG
GGGAGAACACTTCCTGTCCCCTTCAATCTTGTACCAAGTCCAAAATCCTTGCTTTATCTCCTATTGAAATTTA
AGAAATGGATGTGTGAGCTCATCCAGGGTCAAAAGCAAGGCTTCCAAGAAGATGCAGAGATGAACAAGAGAAA
TGAAGAAAAGAAATTTGGAATTTCAGGAAGTCACGAAGACCTTTCAAAATTTTCACTTGACAAAAATCAGTTG
GCACACAACAAACAATCAAGTACAAGGAGCTCAGAAGATTATCATTTAAATAGTTTCAGTAACCCTCCAAGAC
AATATCAGAAAATCATGAAGAGACTCATTAAAAGATATGTATTGCAGGCCCAGATTGATAAGGAGAGCGATGA
GGTGAATGAAGGGGAATTGAAGGAAATTAAGCAAGACATCTCAAGTCTCCGTTATGAACTCCTTGAAGAGAAA
TCACAGAACTCAGAAGACCTAGCAGAGCTCATTAGAAAACTCGGGGAGAGACTGTCGTTAGAGCCAAAGCTGG
AGGAAAGCCGCAGATAGAGCAGAGCCCCTCAGAAGTGCATATTTATTTCTCCACTTGAAGCCATATTATTTTC
TGACTTATTTTTTTAAGTGTCAATGATAAAAAGTATGTTAACTGATAACTTGGATCATTTAGAGTCCTAATAT
CAAGCTTTTTGGGAGATTAAATTGCATTGCTGAGGGCTAACAATTGCTG

FIGURE 3

Gene Sequence Structure * 1497 bp Sequence Deleted 1509 bp

Size of full-length
cDNA: 3261 bp

Targeting Vector*
(genomic sequence)



Arm Length:
5': 3.5 kb
3': 1.5 kb

5'>TCCTCAATTCTAACTGCATTT
CTTCTGGAAAAGAATAAAACGATT
CACCAGAGCTCCAGAGGATAGCCT
AAGCTGAGTTGTTTTTAATCAAAT
CATTCTGTGTGCTGTCTCACCCCT
AGTTTGTGGCTCATCCAAGCTGTC
AGCAACAGCTCCTGTCCATATGGT
ATGAGAACCTCTCTGGTTTACGGC
AGCAGACCATG<3'
(SEQ ID NO:3)

5'>TCGTGGTCCTTGCTGTTGCCA
TTGGATTGCCCTTCCTGGCTCTCA
TATACTGGTGTGCTCCTTGCAGCA
AGGTATGTCTGTGAGTCCTGCAGT
CCATCTGTAGTTGAATTCTGTCCA
GCAGGCAAAGATCTAGCTCCAAAA
TGAAAATATGATTTGAAGTACACA
GGTTCACATAATCTTTCTATTTGT
TTGAGAATTTC<3'
(SEQ ID NO:4)

Targeting Vector
Endogenous Locus

* Not drawn to scale

FIGURE 4

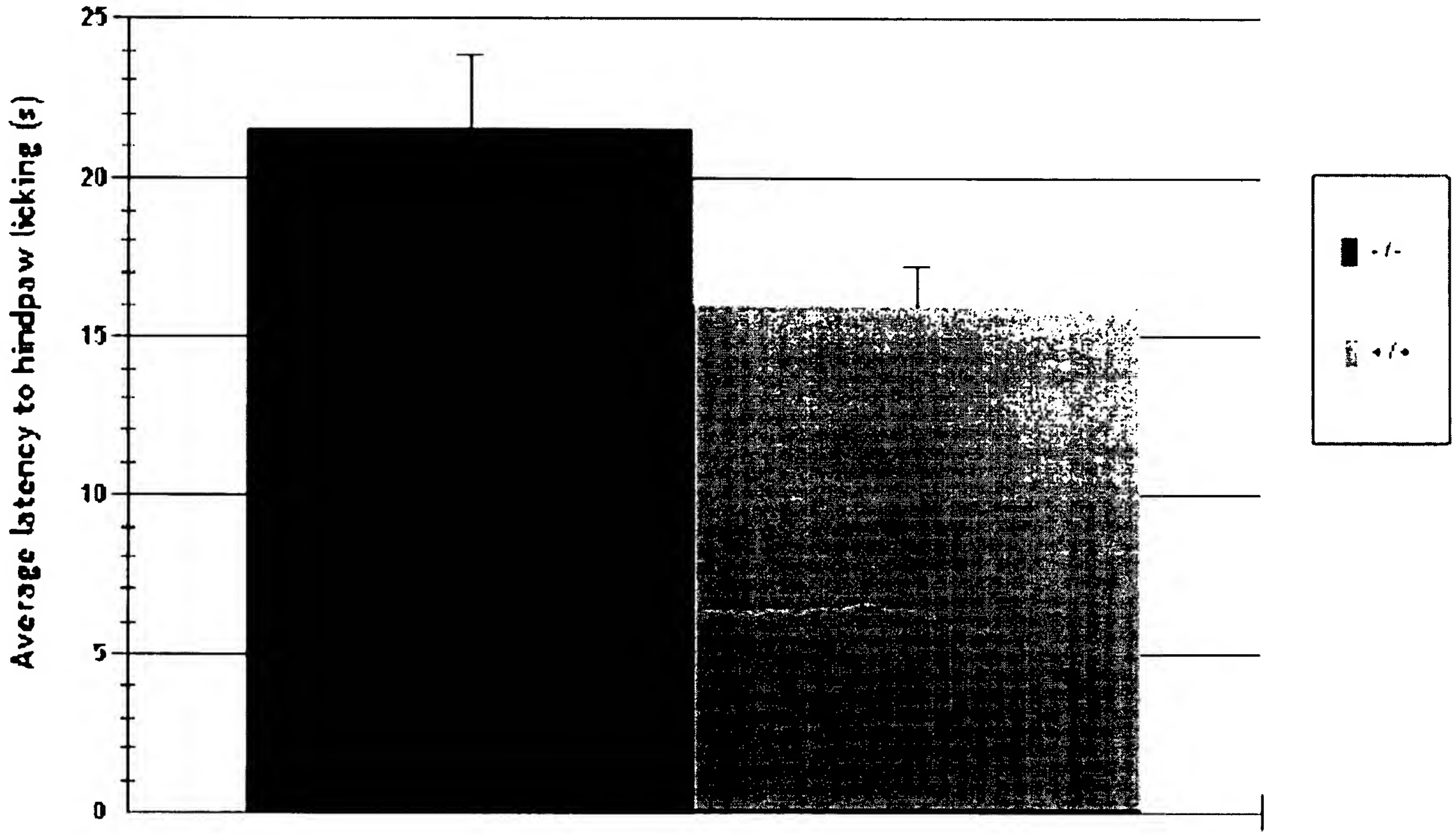


FIGURE 5